

Appl. No. 10/076,967
Amdt. dated April 23, 2007
Amendment under 37 CFR 1.116 Expedited Procedure
Examining Group 1631

PATENTAmendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-54 (canceled)

- 1 55 (currently amended): A method of comparing the correlation between gene
2 and protein expression correlating gene expression with protein expression in two or more
3 biological samples, the method comprising the steps of:
4 a) obtaining two or more biological samples;
5 b) generating a gene expression profile of each sample;
6 c) determining the nucleotide sequence of ~~an~~ at least one mRNA in each gene
7 expression profile;
8 d) predicting the amino acid sequence of the polypeptide encoded by the mRNA
9 in each gene expression profile;
10 e) predicting the mass of the polypeptide encoded by the mRNA in each gene
11 expression profile;
12 f) generating a protein profile of polypeptides in each sample by mass
13 spectrometry; and
14 g) determining the presence ~~or absence~~ in each protein profile of a polypeptide
15 having a mass that ~~correlates to~~ is the same as the predicted mass of the encoded polypeptide,
16 thereby identifying a at least one protein that is ~~or is not~~ expressed from a corresponding mRNA
17 in each biological sample,
18 thereby comparing the correlation between correlating gene expression with and
19 protein expression in two or more biological samples.
- 1 56 (previously presented): The method of claim 55, wherein one of the
2 biological samples comprises a cell lysate from a healthy cell.

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1 57 (previously presented): The method of claim 55, wherein one of the
2 biological samples comprises a cell lysate from a pathological cell.

1 58 (previously presented): The method of claim 55, wherein one of the
2 biological samples comprises a cell lysate from a cell contacted by a toxic compound.

1 59 (previously presented): The method of claim 55, wherein one of the
2 biological samples comprises a cell lysate from a cell of a subject who responds to a drug
3 treatment.

1 60 (previously presented): The method of claim 55, wherein one of the
2 biological samples comprises a cell lysate from a cell of a subject who does not respond to a drug
3 treatment.

1 61 (previously presented): The method of claim 55, wherein the biological
2 samples comprise human cells.

1 62 (previously presented): The method of claim 55, wherein the step of
2 generating the gene expression profile comprises identifying expressed mRNA with a nucleic
3 acid array.

1 63 (previously presented): The method of claim 55, wherein the step of
2 generating the gene expression profile comprises identifying expressed mRNA with an
3 oligonucleotide array.

1 64 (previously presented): The method of claim 55, wherein the step of
2 generating the gene expression profile comprises identifying expressed mRNA with an mRNA
3 array.

1 65 (previously presented): The method of claim 55, wherein the step of
2 generating the gene expression profile comprises identifying expressed mRNA with an EST
3 array.

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1 66 (previously presented): The method of claim 55, wherein the step of
2 generating the gene expression profile comprises identifying expressed mRNA with a northern
3 blot or a dot blot.

67 (canceled)

1 68 (previously presented): The method of claim 55, wherein two biological
2 samples are derived from a normal cell and a pathologic cell.

1 69 (previously presented): The method of claim 68, wherein the pathologic cell
2 is a cancer cell.

1 70 (previously presented): The method of claim 55, wherein two biological
2 samples are derived from a healthy cell and a cell exposed to a toxic compound.

1 71 (previously presented): The method of claim 55, wherein mass spectrometry
2 is laser desorption/ionization mass spectrometry.

1 72 (previously presented): The method of claim 55, wherein mass spectrometry
2 is electrospray mass spectrometry.

1 73 (previously presented): The method of claim 55, further comprising,
2 in step d), after predicting the amino acid sequence of the polypeptide encoded by
3 the mRNA in each gene expression profile, predicting a post-translational modification of the
4 encoded polypeptide;

5 in step e), after predicting the mass of the polypeptide encoded by the mRNA in
6 each gene expression profile, predicting the mass of the encoded polypeptide to reflect the post-
7 translational modification; and

8 in step g), after determining the presence or absence in each protein profile of a
9 polypeptide having a mass that correlates to the predicted mass of the encoded polypeptide,

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10 determining the presence or absence of a polypeptide having a mass that correlates to the
11 predicted mass of the encoded polypeptide having the post-translational modification.

1 74 (previously presented): The method of claim 73, wherein the post-
2 translational modification is phosphorylation or glycosylation.

1 75 (currently amended): The method of claim 55 further comprising:

2 (i) after step [(I)d), predicting at least one physio-chemical characteristic of the
3 polypeptide encoded by the mRNA in each gene expression profile selected from the group
4 consisting of isoelectric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation,
5 epitope sequence, ligand binding sequence, and metal chelate binding;

6 (ii) fractionating the polypeptides in each sample according to the at least one
7 physiochemical characteristic, retaining the fraction containing the predicted physiochemical
8 property, and then generating a protein profile of polypeptides in each sample by mass
9 spectrometry in step [(I)f); and

10 (iii) in step [(I)g), correlating the predicted mass and the at least one
11 physiochemical characteristic of each polypeptide encoded by the mRNA in each gene
12 expression profile with a polypeptide in each respective protein expression profile.

1 76 (previously presented): The method of claim 75, wherein the physio-chemical
2 characteristic is isoelectric point and fractionating the polypeptides comprises isoelectric
3 focusing.

1 77 (previously presented): The method of claim 75, wherein the physiochemical
2 characteristic is isoelectric point and fractionating the polypeptides comprises capturing
3 polypeptides on a solid phase-bound ion exchange adsorbent, washing away unbound
4 polypeptides and detecting the bound polypeptides by laser desorption/ionization mass
5 spectrometry.

1 78 (previously presented): The method of claim 75, wherein the physiochemical
2 characteristic is hydrophobicity and fractionating the polypeptides comprises capturing

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3 polypeptides on a solid phase-bound hydrophobic interaction adsorbent, washing away unbound
4 polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass
5 spectrometry.

1 79 (previously presented): The method of claim 75, wherein the physiochemical
2 characteristic is hydrophilicity and fractionating the polypeptides comprises capturing
3 polypeptides on a solid phase-bound hydrophilic interaction adsorbent, washing away unbound
4 polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass
5 spectrometry.

1 80 (previously presented): The method of claim 75, wherein the physiochemical
2 characteristic is epitope sequence and fractionating the polypeptides comprises capturing
3 polypeptides on a solid phase-bound biospecific adsorbent, washing away unbound polypeptides
4 and detecting the bound polypeptides by laser desoprtion/ionization mass spectrometry.

1 81 (previously presented): The method of claim 75, wherein the physiochemical
2 characteristic is metal chelate binding and fractionating the polypeptides comprises capturing
3 polypeptides on a solid phase-bound immobilized metal chelate adsorbent, washing away
4 unbound polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass
5 spectrometry.